510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
DEVICE ONLY TEMPLATE

A. 510(k) Number:
k033866

B. Analyte:
Benzoylecgonine, amphetamine, opiates, and phencyclidine

C. Type of Test:
Qualitative enzyme immunoassay

D. Applicant:
Lin-Zhi International, Inc.

E. Proprietary and Established Names:
CAMP – Cocaine Metabolite – Amphetamines – Opiate – Phencyclidine – Multiple Analyte Enzyme Immunoassay

F. Regulatory Information:
Regulation section:
21 CFR § 862.3250 (Cocaine and cocaine metabolite test system)
21 CFR § 862.3650 (Opiate test system)
21 CFR § 862.3100 (Amphetamine test system)
Classification:
Class II

1. Product Code:
   DIO (Cocaine and cocaine metabolite test system)
   DJG (Opiate test system)
   DKZ (Amphetamine test system)
   LCM (Phencyclidine test system)
2. Panel:
   Toxicology (91)

G. Intended Use:

1. Intended use(s):
   Refer to Indications for use.

2. Indication(s) for use:

   The Simultaneous Cocaine-Amphetamines-Morphine-Phencyclidine Multiple Analyte Enzyme Immunoassay is a homogeneous enzyme immunoassay with 300 ng/mL cutoff for cocaine metabolite, 1000 ng/mL cutoff for amphetamines, 300 ng/mL cutoff for opiates, and 25 ng/mL cutoff for

phencyclidine. The assay will produce a positive result if any of the four analytes are present at a concentration at or above their respective cutoffs but will not identify which drug is present. The assay is solely intended for the qualitative screening of human urine for these analytes. Measurements obtained by this device are used in the diagnosis and treatment of individuals who have used cocaine, amphetamines, opiates, or phencyclidine. The assay is designed for professional use with a number of automated clinical chemistry analyzers.

The Simultaneous Cocaine-Amphetamines-Morphine-Phencyclidine Multiple Analyte Enzyme Immunoassay provides only a preliminary analytical test result. A more specific alternative chemical method for the individual drugs must be used to obtain a confirmed analytical result. Gas chromatography/mass spectrometry (GC/MS) is the preferred confirmatory method. Clinical consideration and professional judgement should be applied to any drug-of-abuse test result, particularly when preliminary positive results are used.

The device is for in vitro diagnostic use. It is intended for prescription use only.

3. Special condition for use statement(s):

The LZI CAMP Assay provides only a preliminary analytical test result. A positive result indicates that one or more of the four analytes may be present in the sample. In addition, since the assay is designed to detect multiple analytes, it is possible that if two or more analytes are present at concentrations *below* their respective cutoffs, a positive result will be produced. The performance of this assay has been validated using the LZI opiate calibrators only. The sponsor recommends that when the CAMP assay produces a positive result, the sample be retested with individual assays for cocaine metabolite, amphetamines, opiates, and phencyclidine. Following this testing, a more specific alternative chemical method must be used to obtain a confirmed analytical result. Gas chromatography/Mass spectrometry is the preferred confirmatory method. Other chemical confirmation methods are available.

The assay is not designated for use in point-of-care settings.

Tests for opiates cannot distinguish between abused drugs and certain prescribed medications.(e.g., morphine, codeine)

Certain foods or medications may interfere with tests for amphetamines and opiates and cause false positive results.

4. Special instrument Requirements:
   The device is for use on automated clinical chemistry analyzers. Instruments should be capable of maintaining a constant temperature, pipetting samples and reagents, mixing reagents, timing reactions, measuring at 340 nm, and performing standard curve calculations.

   Performance was demonstrated in this submission on the Hitachi 717 analyzer.

H. Device Description:

The device consists of two wet reagents which contain the key components of the immunoassay; a mixture of monoclonal and polyclonal antibodies against the drugs, substrate, and enzyme-labeled drugs (conjugates).

I. Substantial Equivalence Information:

1. Predicate device name(s):
   Cocaine Metabolite Enzyme Immunoassay
   Amphetamines Enzyme Immunoassay
   Opiate Enzyme Immunoassay
   Phencyclidine Enzyme Immunoassay

2. Predicate K number(s):
   k020763
   k020369
   k020368
   k020254
3. Comparison with predicate:

   The CAMP assay is designed to detect all four analytes listed above with a single reagent. The four predicate devices and the CAMP assay are for use on automated analyzers.

   The reagent formulations vary between the new device and the predicate devices.

Similarities		
Item	**Device**	**Predicate**
Methodology	Homogeneous enzyme immunoassay	Same
Benzoylecgonine cutoff	300 ng/mL	Same
Amphetamines cutoff	1000 ng/mL	Same
Opiates cutoff	300 ng/mL	Same
Phencyclidine cutoff	25 ng/mL	Same

Differences		
Item	**Device**	**Predicate**
Assay Type	Qualitative	Qualitative and semi-quantitative
Reagent	Antibodies to benzoylecgonine, amphetamines, opiates, AND phencyclidine	Antibodies to benzoylecgonine, amphetamines, opiates, OR phencyclidine
Controls	8 per run: negative and positive for each of the four analytes	2 per run: negative and positive for the specific analyte
Calibrators	3 per run: negative, cutoff, and high	5 per run: negative, low, cutoff, intermediate, and high for the specific analyte
Sensitivity	Benzoylecgonine: 50 ng/mL Amphetamines: 100 ng/mL Opiates: 50 ng/mL Phencyclidine: 3 ng/mL	Benzoylecgonine: 4 ng/mL Amphetamines: 30 ng/mL Opiates: 15 ng/mL Phencyclidine: 1 ng/mL

J. Standard/Guidance Document Referenced (if applicable):

The sponsor referenced the following guidance document(s) in the submission: Premarket Submission and Labeling Recommendations for Drugs of Abuse Screening Tests - Draft Guidance for Industry and FDA Staff, published December 2003.

K. Test Principle:

The test is an enzyme immunoassay for use on automated clinical chemistry analyzers. The CAMP assay is calibrated with the LZI Opiate Calibrators, at concentrations of 0, 300, and 1000 ng/mL. Enzyme-labeled drug and drug present in the sample compete for limited antibody binding sites. Binding of the enzyme-labeled drug inhibits its reaction with the substrate, thereby influencing the rate of absorbance change measured by the instrument. The rate of absorbance change is proportional to the concentration of drug in the sample. Concentrations of controls and unknowns are calculated from the standard curve.

Results are read at 340 nm.

L. Performance Characteristics (if/when applicable):

Analytical performance:

Precision/Reproducibility:

Samples used for the precision study were the zero calibrator, cutoff calibrator, high calibrator, low control, and high control for cocaine, amphetamines, opiates, and phencyclidine. The study was conducted by one operator using one lot of reagent over eleven days. The assay was calibrated with each analytical run. For within-run precision, each analyte was run 21 times on one day. For between-

run precision, each analyte was run once on day one, then one run per day over the next ten days. Results of the studies are presented below.

Qualitative Precision – Cocaine Metabolite

Sample concentration, ng/mL	Mean mA/min	SD	CV%		Mean mA/min	SD	CV%
Within-Run				Between-Run			
0	736.3	5.49	0.75	0	742.4	3.54	0.48
225	786.2	5.09	0.65	225	793.4	5.13	0.65
300	803.6	7.70	0.96	300	806.9	4.43	0.55
375	811.9	7.02	0.86	375	822.1	7.02	0.85
3000	876.8	5.33	0.61	3000	882.3	5.46	0.62

Qualitative Precision – Amphetamines

Sample concentration, ng/mL	Mean mA/min	SD	CV%		Mean mA/min	SD	CV%
Within-Run				Between-Run			
0	734.7	6.23	0.85	0	742.4	3.54	0.48
750	793.0	6.44	0.81	750	792.8	4.30	0.54
1000	804.0	4.86	0.60	1000	799.0	3.78	0.47
1250	810.2	5.94	0.73	1250	808.9	6.14	0.76
2000	825.5	5.73	0.69	2000	828.4	3.31	0.40

Qualitative Precision – Opiates

Sample concentration, ng/mL	Mean mA/min	SD	CV%		Mean mA/min	SD	CV%
Within-Run				Between-Run			
0	736.0	6.62	0.90	0	742.4	3.54	0.48
225	782.4	7.20	0.92	225	793.0	6.45	0.81
300	801.8	7.35	0.92	300	809.1	4.55	0.56
375	817.5	6.35	0.78	375	819.8	3.05	0.37
1000	878.7	5.85	0.67	1000	886.0	6.15	0.69

Qualitative Precision – Phencyclidine

Sample concentration, ng/mL	Mean mA/min	SD	CV%		Mean mA/min	SD	CV%
Within-Run				Between-Run			
0	735.1	6.16	0.84	0	742.4	3.54	0.48
18	789.6	6.14	0.78	18	794.1	5.03	0.63
25	799.2	5.24	0.66	25	804.9	5.11	0.63

32	809.3	7.01	0.87	32	814.0	4.63	0.57
100	833.5	6.33	0.76	100	829.1	4.68	0.56

Precision Study Results Around the Cutoff

		COC		**AMP**	
Cutoff Rate (mA/min)		812.3		813.2	
Cutoff Concentration		300 ng/mL		1000 ng/mL	
Concentration of sample, ng/mL	Replicate	Rate (mA/min)	Result	Rate (mA/min)	Result
Spiked near cutoff – 25%	1	803.8	Neg	797.5	Neg
	2	808.0	Neg	806.6	Neg
	3	800.7	Neg	801.3	Neg
	4	809.0	Neg	789.4	Neg
	5	803.6	Neg	807.6	Neg
Spiked near cutoff + 25%	1	829.7	Pos	825.3	Pos
	2	826.4	Pos	821.2	Pos
	3	821.5	Pos	820.3	Pos
	4	820.4	Pos	818.2	Pos
	5	827.3	Pos	817.9	Pos

		OP		**PCP**	
Cutoff Rate (mA/min)		816.6		817.0	
Cutoff Concentration		300 ng/mL		25 ng/mL	
Concentration of sample, ng/mL	Replicate	Rate (mA/min)	Result	Rate (mA/min)	Result
Spiked near cutoff – 25%	1	807.6	Neg	804.4	Neg
	2	803.3	Neg	802.7	Neg
	3	798.9	Neg	799.5	Neg
	4	805.3	Neg	808.4	Neg
	5	800.2	Neg	804.6	Neg
Spiked near cutoff + 25%	1	837.0	Pos	830.2	Pos
	2	826.6	Pos	831.5	Pos
	3	843.6	Pos	824.0	Pos
	4	825.8	Pos	832.3	Pos
	5	848.7	Pos	820.6	Pos

Linearity/assay reportable range:

Not applicable. The assay is intended for qualitative use.

Traceability (controls, calibrators, or method):

Calibrators and commercial control materials are specified in the labeling but are not supplied in the kit. The calibrators were previously cleared under premarket notification K020368. Controls were cleared under K020763, K020369, K020368, and K020254.

Detection limit:

Sensitivity of the assay to the four analytes is as follows:

Cocaine metabolite – 50 ng/mL
Amphetamine/Methamphetamine – 100 ng/mL
Opiates – 50 ng/mL
Phencyclidine – 3 ng/mL

To determine analytical sensitivity, the sponsor assayed the zero calibrator 10 times within the same run and calculated the average and standard deviation of those readings in mA/min. Two standard deviations were then added to the average of the readings. This represented the sponsor's estimate of the absorbance rate corresponding to the analytical sensitivity of the assay. The estimated absorbance rate was then compared to the measured absorbance rate of the proposed sensitivity for that analyte. If the estimated absorbance rate was less than the measured absorbance rate, the sensitivity of the assay was considered to be less than or equal to the concentrations listed above.

Analytical specificity:

Cross-reactivity was established by spiking various concentrations of similarly structured drug compounds into the zero calibrator. By analyzing various concentration of each compound the sponsor determined the concentration of the drug that produced a response approximately equivalent to the cutoff concentration of the assay. Results of those studies appear in the table(s) below:

Amphetamine/Methamphetamine

Drug Compound	Response equivalent to cutoff in ng/mL
d-amphetamine	1000
l-amphetamine	Neg up to 24, 000 ng/mL
d-methamphetamine	1000
l-methamphetamine	Neg up to 10, 000 ng/mL
D,L 3,4-Methylenedioxymethamphetamine (MDMA)	2500
3,4-Methylenedioxyamphetamine (MDA)	2800

Opiates

Drug compound	Response equivalent to cutoff in ng/mL
Codeine	150
Norcodeine	7000
Hydrocodone	300
Hydromorphone	600
Oxycodone	2000
Thebaine	400
Oxymorphone	6000
Morphine	300
Morphine-3-β-glucuronide	625
Morphine-6-β-glucuronide	550
Dihydrocodeine	400
Levorphanol	600

Cocaine

Compound	Response equivalent to cutoff in ng/mL
Benzoylecogonine	300
Cocaine	30,000
Norcocaine	60,000
Ecgonine Methyl Ester	350,000

Phencyclidine

Phencyclidine	25

The following compounds were evaluated for potential positive interference with the assay. To evaluate for interference test compounds were spiked into the drug-free calibrator at various concentrations listed below. None of the compounds on the list caused a positive result with the CAMP assay.

Compounds	Conc. (ug/ml)	X-reactivity
Acetaminophen	1500	Negative
Acetylsalicyclic Acid	1500	Negative
Albuterol	3000	Negative
Amitriptyline	50	Negative
l-Amphetamine	24	Negative
Amobarbital	1000	Negative
Benzphetamine	2000	Negative
Bromopheniramine	100	Negative
Bupropion	1000	Negative
Buspirone	3000	Negative
Caffeine	100	Negative
Chlorpheniramine	50	Negative
Chlorpromazine	80	Negative
Clomipramine	30	Negative
Cycloazocine	300	Negative
Desipramine	130	Negative
Dextromethorphan	40	Negative
Diphenhydramine	100	Negative
Doxepin	175	Negative

d,l-Ephedrine	700	Negative
Fenfluramine	7	Negative
Fentanyl	3000	Negative
Fluoxetine	800	Negative
Fluphenazine	3000	Negative
Isoxsuprine	3000	Negative
Imipramine	20	Negative
Ketamine	100	Negative
Lidocaine	1000	Negative
Maprotiline	600	Negative
Meperidine	25	Negative
Methadone	1000	Negative
Mephentermine	50	Negative
Methapyrilene	300	Negative
Metronidazole	700	Negative
Nalbuphine	3000	Negative
Nicotine	800	Negative
Norpropoxyphene	100	Negative
Nortriptyline	100	Negative
Oxazepam	1000	Negative
Phendimetrazine	300	Negative
Phenethylamine	40	Negative
Phenmetrazine	75	Negative
Phenobarbital	1000	Negative
Phenothiazine	100	Negative
Phentermine	40	Negative
Phenylephrine	500	Negative
d-Phenylpropanolamine	2500	Negative
d,l-Phenylpropanolamine	500	Negative
l-Phenylpropanolamine	240	Negative
Primidone	1000	Negative
Procainamide	800	Negative
Promethazine	100	Negative
Propoxyphene	260	Negative
Propranolol	100	Negative
d-Pseudoephedrine	250	Negative
l-Pseudoephedrine	2500	Negative
Ranitidine	800	Negative
Scopolamine	3000	Negative
Secobarbital	1000	Negative
Sertraline	1000	Negative
Thioridazine	70	Negative
Tramadol	1000	Negative
Trazodone	2900	Negative
Trifluoperazine	3000	Negative
Triflupromazine	3000	Negative
Triprolidine	150	Negative
Tyramine	600	Negative
Valproic Acid	1000	Negative

The sponsor did not evaluate the effects of pH, specific gravity, or albumin on the assay.

There is the possibility that other substances and/or factors not listed above may interfere with the test and cause false results, e.g., technical or procedural errors.

Assay cut-off:

The identified cutoff concentrations of the assays are recommended for use by the Substance Abuse and Mental Health Services Administration (SAMHSA), except for the opiate assay.

Characterization of how the device performs analytically around the claimed cutoff concentration appears in the precision section, above.

Comparison studies:

Method comparison with predicate device:

Samples previously analyzed by GC-MS were selected to be analyzed by the candidate device. Some samples were prepared by diluting clinical samples with high drug concentrations with drug-free urine. This was done in order to obtain samples near the cutoff concentration of the assay, because the sponsor was not able to obtain unaltered samples near the cutoff.

For the method comparison studies, the following sample groups were selected, for a total of n = 170.

Benzoylecgonine group: 40 samples
Amphetamines group: 40 samples
Opiates group: 32 samples
Phencyclidine group: 38 samples
Negative for all analytes: 20 samples

The BE, AMP, OP, and PCP samples were analyzed by the candidate device and predicate devices and are traceable to GC-MS concentrations. The samples negative for all analytes were analyzed by the candidate device and the predicate devices only.

The study included an adequate number of samples that contained drugs near to the cutoff concentration of the assay. More than 10% of the study samples are evenly distributed between plus and minus 50% of the claimed cutoff concentration of each analyte.

The study was performed at the manufacturer's facility by the manufacturer's staff.

Candidate Device Results vs. Predicate Device Results (four analytes)

	Positive by Predicate Devices	Negative by Predicate Devices
Positive by Candidate Device	75	0
Negative by Candidate Device	0	95

Agreement among positives is 100%
Agreement among negatives is 100%

Candidate Device Results vs. stratified GC/MS Values
Benzoylecgonine

Candidate Device Results	**Negative** by the predicate device or less than half the cutoff concentration by GC/MS analysis	**Near Cutoff Negative** (Between 50% below the cutoff and the cutoff concentration)	**Near Cutoff Positive** (Between the cutoff and 50% above the cutoff concentration)	**High Positive** (greater than 50% above the cutoff concentration)
Positive	0	0	12	8
Negative	6	14	0	0

Agreement among positives is 100%
Agreement among negatives is 100%

Candidate Device Results vs. stratified GC/MS Values
Amphetamines

Candidate Device Results	**Negative** by the predicate device or less than half the cutoff concentration by GC/MS analysis	**Near Cutoff Negative** (Between 50% below the cutoff and the cutoff concentration)	**Near Cutoff Positive** (Between the cutoff and 50% above the cutoff concentration)	**High Positive** (greater than 50% above the cutoff concentration)
Positive	0	1	11	8
Negative	5	14	1	0

Agreement among positives is 95%
Agreement among negatives is 95%

Candidate Device Results vs. stratified GC/MS Values
Opiates

Candidate Device Results	**Negative** by the predicate device or less than half the cutoff concentration by GC/MS analysis	**Near Cutoff Negative** (Between 50% below the cutoff and the cutoff concentration)	**Near Cutoff Positive** (Between the cutoff and 50% above the cutoff concentration)	**High Positive** (greater than 50% above the cutoff concentration)
Positive	1	0	9	6
Negative	2	13	1	0

Agreement among positives is 94%; Agreement among negatives is 94%

Candidate Device Results vs. stratified GC/MS Values

Phencyclidine

Candidate Device Results	**Negative** by the predicate device or less than half the cutoff concentration by GC/MS analysis	**Near Cutoff Negative** (Between 50% below the cutoff and the cutoff concentration)	**Near Cutoff Positive** (Between the cutoff and 50% above the cutoff concentration)	**High Positive** (greater than 50% above the cutoff concentration)
Positive	0	0	12	7
Negative	5	14	0	0

Agreement among positives is 100%
Agreement among negatives is 100%

GC/MS values used to categorize samples in these tables are based on:
Cocaine group: benzoylecgonine only
Amphetamines group: sum of amphetamine and methamphetamine
Opiates group: sum of morphine, codeine, and hydromorphone
Phencyclidine group: phencyclidine only

Matrix comparison:

Not applicable. The assay is intended for only one sample matrix.

3. Clinical studies:
   a. *Clinical sensitivity:*
      Not applicable. Clinical studies are not typically submitted for this device type.
   b. *Clinical specificity:*
      Not applicable. Clinical studies are not typically submitted for this device type.
   c. *Other clinical supportive data (when a and b are not applicable):*

4. Clinical cut-off:
   Not applicable.
5. Expected values/Reference range:
   Not applicable.

M. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.